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10/508,337	04/25/2005	Yoshiaki Kawashima	12480-000063/US	5676

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EXAMINER	
HELM, CARALYNNE E	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
03/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,337	KAWASHIMA ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,23-42 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 17-21, 23-30, 31-42, and 45* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/01/04, 9/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election **without** traverse of Group I in the reply filed on January 4, 2008 is acknowledged. The claims drawn to the nonelected invention were cancelled by the applicant. The restriction is deemed proper and thereby made FINAL.

Abstract

The abstract of the disclosure is objected to because it exceeds the 150 word limit. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract *not exceed 150 words in length* since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The language should be clear and concise and should not repeat information given in the title. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

Claim Objections

Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. The claim recites the use of an aqueous binder in a dry (e.g. void of liquid) granulation process.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 12, 13, 17, 20, 21, 23, 28, 37, 38, 40, 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejected claims each recite a method step performed "in accordance with" a particular process. For example, instant claim 12 recites the method step of "forming the nano particles in accordance with" the process of "spherical granulation". The metes and bounds of the phrase "in accordance with" are not defined or established by the specification. Generally the phrase "in accordance with" means "agrees with". Thus this claim simply states that the process used to form the nano particles must agree with spherical crystallization in some sense; it then follows that any process that produces a nano particle is in agreement with spherical crystallization, since both result in the formation of a nano particle. Therefore, the phrase "in accordance with" can be interpreted as meaning "optionally" and this interpretation is used in the subsequent claim rejections based upon prior art.

Claims 17 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both claims depend from a claim that recites a method of combining primary particles with each other (claim 11). Claims 17 and 40 confusingly add the limitation of performing this combination step by adhering the primary particles to a carrier. It is unclear if the primary particles are adhered to a carrier individually OR if the combination of the primary particles with just each other and adherence to a carrier happens simultaneously OR if some other embodiment was intended. If the intent was to have the former, where the primary particles are adhered individually to a carrier, then claims 17 and 40 are not further limiting. If on the other hand, the intent was to have the primary particles combine just with each other and adhere to a carrier, simultaneously, then the claims would not be fully enabled. For the sake of applying prior art, both claims are viewed as reciting a combining step where primary particles are adhered to the surface of carrier particles (e.g. the combining step of the dependent claims is viewed as superseding/replacing the combining step of the independent claim from which they depend).

Claims 7 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite a ratio that is presented as a weight percent, with no basis or point of comparison. Thus it is unclear as to whether the drug ratio/percent is based upon the total weight of the particle, the other materials in the particle, or some other basis.

Claim 28 and 29 recite the limitation "the lubricant powder" and "the polymer nano particle. There is insufficient antecedent basis for these limitations in the claim since claim 23, the claim form which both the instant claims depend, recites neither a lubricant powder nor a polymer nano particle.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Ohkuma et al (U.S. Patent No. 7,022,311).

Ohkuma et al. teach a method of making a composite drug particle by dry mechanical means where powdered forms of an active ingredient (drug) and carrier particles are combined (see column 7 lines 60- column 8 line 2, claims 4 and 16). Therefore claim 1 is unpatentable over Ohkuma et al.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 8, 33, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishizaka et al. (U.S Patent no. 5,336,271 – see 892).

Ishizaka et al. teach a method of making a composite particle made by the combination of a drug powder and a core particle powder by mechanical impact (see column 4 lines 25-29, column 6 lines 3-5 and 12, and column 7 lines 37-42; instant claim 1). Ishizaka et al. further

teach that the core particle (diluting agent powder) is starch and that its size is 15 μm (see column 4 lines 25-29 and column 7 lines 37-42; instant claims 2-3, 5, and 33). In addition, Ishizaka et al. also teach that the drug is an antipyretic (see column 4 lines 25-29; instant claims 8 and 36). Therefore claims 1-3, 5, 8, 33, and 36 are unpatentable over Ishizaka et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The four factual inquires of Graham v. John Deere Co. have been fully considered and analyzed in the rejections that follow.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 4, 6, 9, 32, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al.

Ishizaka et al. teach a method of making a composite particle made by dry mechanical impact of powdered forms of a drug, starch, and polyethylene glycol (biocompatible polymer) (see column 4 lines 25-29; instant claim 9). Ishizaka et al. go on to teach that the starch, as the parent or core particle, ranges in size from 0.5μm to 1mm and that the child particles (drug and polyethylene glycol) that are fixed to the surface are smaller in size (see column 3 lines 57-58 and column 4 lines 40-47; instant claim 9). Thus, when the size of the starch particles is in the lower end of the range (e.g. 0.5μm) the drug and polyethylene glycol particles are less than 500nm in size (see instant claims 4, 6, 9, 32, and 34). Further it would have been well within the purview of one of ordinary skill in the art at the time the invention was made to modify the size of the drug particles relative to the starch as a matter of routine optimization. Therefore claims 4, 6, 9, 32, and 34 are obvious over Ishizaka et al.

Claims 10-15 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trofast et al. (WO 95/09616) in view of Jain et al. (U.S. Patent No. 6,165,506).

Trofast et al. teach a method of agglomerating fine drug particles via a dry process such that the agglomerated particles (composite particles) would be able to break up into their substituent particles during inhalation (page 2 lines 10-21, page 4 lines 7-8, page 5 lines 6-9; instant claim 10). Trofast et al. do not specifically teach that the fine drug particles are less than 1000nm; however, Jain et al. teach that drug particles sized less than 1000nm were known in

the art at the time of the invention for use in solid dosage forms due to their improved dissolution profile (see column 2 line 51-column 3 line 2; instant claims 10 and 11). It would therefore have been obvious to one of ordinary skill in the art at the time of the invention to use particles less than 1000nm in size in the method of Trofast et al. The limitations of instant claims 12 and 37 would also have been met by this artisan of ordinary skill at the time of invention since a method of producing a nano particle is implicitly present when particles less than 1000nm in size are used in the agglomeration method of Trofast et al. Furthermore, since the formation agglomerates form any particle less than 10 μm in size was known, it also would have been obvious to one of ordinary skill in the art at the time of the invention to use the agglomerates formed by Trofast et al. (using nano particles) as the starting material in their agglomeration process (see page 2 lines 10-13; instant claims 13 and 38). Additionally, Trofast et al. teach that the agglomerates (primary particles) can be subjected to a secondary granulation process (see page 11 line 13- page 12 line 2 and page 12 lines 16-17 and figure 5; instant claims 13 and 38). Trofast also teaches that a binder can be used in their agglomeration process as well as additional ingredients other than the drug (see page 2 lines 10-14 and page 4 lines 26-30; instant claims 15 and 39). Further, Trofast et al. teach that the agglomeration process is performed by systematic agitation (fluid bed dry granulation) of powdered material to be formed into agglomerates (see page 2 lines 10-14; instant claims 15 and 39). The size of the agglomerates (primary particles) is a parameter that would depend on the particular processing equipment and other manufacturing conditions whose optimization would be well within the purview of one of ordinary skill in the art at the time the invention was made (see instant claim 14). Therefore claims 10-15 and 37-39 are obvious over Ishizaka et al. in view of Jain et al.

Claims 10, 17-19, and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al. in view of Trofast et al. and Jain et al.

Trofast et al. in view of Jain et al. make obvious a dry method of making agglomerate particles composed of nano particles (see ***Claim Rejections - 35 USC § 103*** for claims 10-15 and 37-39 above; instant claim 10). Ishizaka et al. teach a composite particle made by the combination of a drug powder and a core particle powder by mechanical impact (see column 4 lines 25-29, column 6 lines 3-5 and 12, and column 7 lines 37-42; instant claim 17). Ishizaka et al. go on to teach that the starch, as the parent or core particle, ranges in size from 0.5μm to 1mm and that the child particles(drug) that are fixed to the surface are smaller in size (see column 3 lines 57-58 and column 4 lines 40-47; instant claims 18-19 and 40-41). Thus, when the size of the starch particles is in the lower end of the range (e.g. 0.5μm) the drug particles are less than 500nm in size. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the agglomerate particles composed of drug nano particles taught by Trofast et al. modified by Jain et al. (for their improved dissolution profile as taught by Jain et al. column 2 lines 51-59), as the drug/child particles in Ishikawa et al. As optimization of the sizing of the various particles and agglomerates would have been a parameter well within the purview of one of ordinary skill in the at the time of the invention, claims 17-19 and 40-41 are obvious over Ishikawa et al. in view of Trofast et al. and Jain et al.

Claims 10, 17-18, 20-21, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al. in view of Trofast et al., Jain et al., and Bruno et al. (U.S. Patent No. 5, 518, 187).

Ishizaka et al. in view of Trofast et al., Jain et al. make obvious the limitations of claims 10, 17 and 18. This modified reference does not teach surface modification of the carrier using

other particles. Bruno et al. teach that milling is used to modify the surface properties to improve the dissolution properties of particles used in pharmaceuticals (see column 1 lines 9-14). Further Bruno et al. teach using other particles that are often used as lubricants (e.g. copolymers of lactide and glycolide) to mill (modify the surface) the particles used in pharmaceutical preparations (see column 1 lines 61-64 and column 2 lines 48, 52, and 12-14; instant claims 20-21 and 42). It would have been obvious to one of ordinary skill in the art to use the milling method of Bruno et al. to improve the dissolution properties in the composite particle made by the method of Ishizaka et al. modified by Trofast et al and Jain et al. Therefore claims 10, 17-18, 20-21, and 42 are obvious over Ishizaka et al. in view of Trofast et al., Jain et al., and Bruno et al.

Claims 23-27, 30, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizaka et al. in view of Jain et al., Ryde et al., and Zhu et al. 9U.S. PGPub No. 2002/0119117).

Ishizaka et al. teach a dry method of making a composite particle with a parent or core particle, which ranges in size from 0.5μm to 1mm, and smaller child particles that are fixed to the surface (see column 3 lines 57-58, column 4 lines 40-47, and column 6 lines 3-5 and 12-13; instant claim 23). Ryde et al. teach the production of a composite pharmaceutical where a surface stabilizer (lubricant) is adsorbed to the surface of a drug and both are sized such that the composite is less than about a 1μm in size (e.g. both the drug and surface stabilizer are less than 1μm in size) (see column 6 lines 24-33 and column 7 lines 32-34; instant claims 23, 24, 28, 30, and 45– use of nano particle implicitly requires a step of producing the nano particle). Jain et al. teach the production of a nanoscale composite pharmaceutical where a surface modifier (lubricant) is adsorbed to the surface of a drug (see column 2 line 66-column 3 line 2; instant

claims 23 and 24). Thus in order to exploit the improved dissolution properties of nanoscale pharmaceutical components, one of ordinary skill in the art at the time the invention was made would have found it obvious to use the method of Ishikawa et al. to produce a composite particle where a drug served as the parent and a lubricant served as a the child, such that the lubricant was less than 1000nm. Jain et al. teach that calcium stearate can be used as a surface modifier (see page 5 lines 48, 56, and 65-66; instant claims 25 and 27). Ryde et al. teach that magnesium stearate and calcium stearate are both used as lubricants in pharmaceutical preparations (see column 10 lines 45-47 and 49-50; instant claims 25 and 27). Thus it would have been obvious to one of ordinary skill in the art to use magnesium stearate as the lubricant powder adhered to the drug parent particles. Finally, Zhu et al. teach the use of silica gel (colloidal silica) to encapsulate drug for aerosol administration, requiring the composite particles to be less than 5 μm in diameter (see paragraphs 2, 38, and 48; instant claims 25-26). It therefore also would have been obvious to one of ordinary skill in the art at the time the invention was made to use colloidal silica as the child/lubricant powder adhered to the drug parent particles. Therefore, claims 23-27, 30, and 45 are obvious over Ishizaka et al. in view of Jain et al., Ryde et al., and Zhu et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 23-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12 and 16 of U.S. Patent No. 7,022,311. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim a dry process of making a composite particle with a drug and carrier/surface modifier/nano particle where the carrier is taught be less than 1000nm (see claim 17). It would have been obvious to one of ordinary skill in the art to use the teachings in claim 17 of Patent No. 7,022,311 to practice the method of claims 12 and 16. Therefore, instant claims 1 and 23-24 are obvious over claims 12 and 16 of U.S. Patent No. 7,022,311.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Thursday 8-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael P Woodward/
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